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# Updated Recommendations for Use of Tetanus Toxoid, Reduced Diphtheria Toxoid and Acellular Pertussis Vaccine (Tdap) in Pregnant Women and Persons Who Have or Anticipate Having Close Contact with an Infant Aged <12 Months --- Advisory Committee on Immunization Practices (ACIP), 2011

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Compared with older children and adults, infants aged <12 months have substantially higher rates of pertussis and the largest burden of pertussis-related deaths. Since 2004, a mean of 3,055 infant pertussis cases with more than 19 deaths has been reported each year through the National Notifiable Diseases Surveillance System (CDC, unpublished data, 2011). The majority of pertussis cases, hospitalizations, and deaths occur in infants aged ≤2 months, who are too young to be vaccinated; therefore, other strategies are required for prevention of pertussis in this age group. Since 2005, the Advisory Committee on Immunization Practices (ACIP) has recommended tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) booster vaccines to unvaccinated postpartum mothers and other family members of newborn infants to protect infants from pertussis, a strategy referred to as cocooning (*1*). Over the past 5 years, cocooning programs have proven difficult to implement widely (*2,3*). Cocooning programs might achieve moderate vaccination coverage among postpartum mothers but have had limited success in vaccinating fathers or other family members. On June 22, 2011, ACIP made recommendations for use of Tdap in unvaccinated pregnant women and updated recommendations on cocooning and special situations. This report summarizes data considered and conclusions made by ACIP and provides guidance for implementing its recommendations.

ACIP recommends a single Tdap dose for persons aged 11 through 18 years who have completed the recommended childhood diphtheria and tetanus toxoids and pertussis/diphtheria and tetanus toxoids and acellular pertussis (DTP/DTaP) vaccination series and for adults aged 19 through 64 years who have not previously received Tdap (*1,4*). ACIP also recommends that adults aged 65 years and older receive a single dose of Tdap if they have or anticipate having close contact with an infant aged <12 months and previously have not received Tdap (*5*). Two Tdap vaccines are available in the United States. Adacel (Sanofi Pasteur) is licensed for use in persons aged 11 through 64 years. Boostrix (GlaxoSmithKline Biologicals) is licensed for use in persons aged ≥10 years (*6*).

The ACIP Pertussis Vaccines Work Group reviewed unpublished Tdap safety data from pregnancy registries and the Vaccine Adverse Event Reporting System (VAERS) and published studies on use of Tdap in pregnant women. The Work Group also considered the epidemiology of pertussis in infants and provider and program feedback, and then presented policy options for consideration to ACIP. These

updated recommendations on use of Tdap in pregnant women are consistent with the goal of reducing the burden of pertussis in infants.

### Safety of Tdap in Pregnant Women

In prelicensure evaluations, the safety of administering a booster dose of Tdap to pregnant women was not studied. Because information on use of Tdap in pregnant women was lacking, both manufacturers of Tdap established pregnancy registries to collect information and pregnancy outcomes from pregnant women vaccinated with Tdap. Data on the safety of administering Tdap to pregnant women are now available. ACIP reviewed published and unpublished data from VAERS, Sanofi Pasteur (Adacel) and GlaxoSmithKline (Boostrix) pregnancy registries, and small studies (*7,8*). ACIP concluded that available data from these studies did not suggest any elevated frequency or unusual patterns of adverse events in pregnant women who received Tdap and that the few serious adverse events reported were unlikely to have been caused by the vaccine. Both tetanus and diphtheria toxoids (Td) and tetanus toxoid vaccines have been used extensively in pregnant women worldwide to prevent neonatal tetanus. Tetanus- and diphtheria-toxoid containing vaccines administered during pregnancy have not been shown to be teratogenic (*9,10*). From a safety perspective, ACIP concluded that administration of Tdap after 20 weeks' gestation is preferred to minimize the risk for any low-frequency adverse event and the possibility that any spurious association might appear causative.

### Transplacental Maternal Antibodies

For infants, transplacentally transferred maternal antibodies might provide protection against pertussis in early life and before beginning the primary DTaP series. Several studies provide evidence supporting the existence of efficient transplacental transfer of pertussis antibodies (*7,11,12*). Cord blood from newborn infants whose mothers received Tdap during pregnancy or before pregnancy had higher concentrations of pertussis antibodies when compared with cord blood from newborn infants of unvaccinated mothers (*7,11*). The half-life of transferred maternal pertussis antibodies is approximately 6 weeks (*12*). The effectiveness of maternal antipertussis antibodies in preventing infant pertussis is not yet known, but pertussis-specific antibodies likely confer protection and modify the severity of pertussis illness (*13,14*). In addition, a woman vaccinated with Tdap during pregnancy likely will be protected at time of delivery, and therefore less likely to transmit pertussis to her infant. After receipt of Tdap, boosted pertussis-specific antibody levels peak after several weeks, followed by a decline over several months (*15,16*). To optimize the concentration of maternal antibodies transferred to the fetus, ACIP concluded that unvaccinated pregnant women should receive Tdap, preferably in the third or late second (after 20 weeks gestation) trimester.

### Interference with Infant Immune Response to Primary DTaP Vaccination

Several studies have suggested that maternal pertussis antibodies can inhibit active pertussis-specific antibody production after administration of DTaP vaccine to infants of mothers vaccinated with Tdap during pregnancy, referred to as blunting (*12,17*). Because correlates of protection are not fully understood, the clinical importance of blunting of an infant's immune response is not clear. Evidence suggests that any blunting would be short-lived because circulating maternal antibodies decline rapidly (*12,18*). Circulating maternal pertussis antibodies might reduce an infant's risk for pertussis in the first few months of life but slightly increase risk for disease because of a blunted immune response after receipt of primary DTaP doses. The benefit would be to reduce the risk for disease and death in infants aged <3 months, but the trade-off might be to increase the occurrence of pertussis in older infants; however, this group experiences a substantially lower burden of hospitalizations and mortality (National Notifiable Diseases Surveillance System, CDC, unpublished data, 2011).

Currently, two clinical trials are being conducted to measure the immune response of infants receiving DTaP immunization at ages 2, 4, and 6 months whose mothers received Tdap during the third trimester of pregnancy (*19,20*). These trials also are designed to evaluate safety and immunogenicity of Tdap

during pregnancy, but are not sufficiently powered to assess disease endpoints. Analysis of interim data from one trial (*19,* unpublished data) measured infant antibody to pertussis antigens in a blinded fashion for two groups: infants whose mothers received Tdap and infants whose mothers received Td. The first group had elevated antipertussis antibody levels compared with the second at birth and before dose 1, which might be the result of passive antibody transfer, but had lower antipertussis antibody levels after dose 3. In both groups, antipertussis antibody levels were comparable before doses 2 and 3. Although the first group had lower antipertussis antibody levels after dose 3, the evidence of sufficient immune response to DTaP doses compared with the second group was reassuring. ACIP concluded that the interim data are consistent with previously published literature suggesting a short duration of blunting of the infant response, and that the potential benefit of protection from maternal antibodies in newborn infants outweighs the potential risk for shifting disease burden to later in infancy.

### Cocooning

Cocooning is defined as the strategy of vaccinating pregnant women immediately postpartum and all other close contacts of infants aged <12 months with Tdap to reduce the risk for transmission of pertussis to infants. Cocooning has been recommended by ACIP since 2005. Cocooning programs have achieved moderate postpartum coverage among mothers but have had limited success in vaccinating fathers or other family members (*3*) (CDC, unpublished data, 2011). Programmatic challenges make implementation of cocooning programs complex and also impede program expansion and sustainability (*2*). The effectiveness of vaccinating postpartum mothers and close contacts to protect infants from pertussis is not yet known, but the delay in antibody response among those vaccinated with Tdap after an infant's birth might result in insufficient protection to infants during the first weeks of life (*21*). ACIP concluded that cocooning alone is an insufficient strategy to prevent pertussis morbidity and mortality in newborn infants. Regardless, ACIP concluded that cocooning likely provides indirect protection to infants and firmly supports vaccination with Tdap for unvaccinated persons who anticipate close contact with an infant.

### Decision and Cost Effectiveness Analysis

A decision analysis and cost effectiveness model was developed to assess the impact and cost effectiveness of maternal Tdap vaccination during pregnancy compared with immediately postpartum. The model showed that Tdap vaccination during pregnancy would prevent more infant cases, hospitalizations, and deaths compared with the postpartum dose for two reasons: 1) vaccination during pregnancy benefits the mother and infant by providing earlier protection to the mother, thereby protecting the infant at birth; and 2) vaccination during late pregnancy maximizes transfer of maternal antibodies to the infant, likely providing direct protection to the infant for a period after birth. Model results were most sensitive to efficacy of maternal antibodies and risk for disease as a result of blunting; however, a sensitivity analysis in which infants were assumed to have as little as 20% efficacy of maternal antibodies and a 60% increase in risk for disease as a result of blunting found that maternal vaccination during pregnancy was more cost effective and prevented a greater proportion of infant cases and deaths than postpartum maternal vaccination (*22*).

### Guidance for Use

**Maternal vaccination.** ACIP recommends that women's health-care personnel implement a Tdap vaccination program for pregnant women who previously have not received Tdap. Health-care personnel should administer Tdap during pregnancy, preferably during the third or late second trimester (after 20 weeks' gestation). If not administered during pregnancy, Tdap should be administered immediately postpartum.

**Cocooning.** ACIP recommends that adolescents and adults (e.g., parents, siblings, grandparents, child-care providers, and health-care personnel) who have or anticipate having close contact with an infant aged <12 months should receive a single dose of Tdap to protect against pertussis if they have not

previously received Tdap. Ideally, these adolescents and adults should receive Tdap at least 2 weeks before beginning close contact with the infant.

**Special Situations**

**Pregnant women due for tetanus booster.** If a tetanus and diphtheria booster vaccination is indicated during pregnancy for a woman who has previously not received Tdap (i.e., more than 10 years since previous Td), then Tdap should be administered during pregnancy, preferably during the third or late second trimester (after 20 weeks' gestation).

**Wound management for pregnant women.** As part of standard wound management care to prevent tetanus, a tetanus toxoid--containing vaccine might be recommended for wound management in a pregnant woman if 5 years or more have elapsed since last receiving Td. If a tetanus booster is indicated for a pregnant woman who previously has not received Tdap, Tdap should be administered.

**Pregnant women with unknown or incomplete tetanus vaccination.** To ensure protection against maternal and neonatal tetanus, pregnant women who have never been vaccinated against tetanus should receive three vaccinations containing tetanus and reduced diphtheria toxoids. The recommended schedule is 0, 4 weeks, and 6 to 12 months. Tdap should replace 1 dose of Td, preferably during the third or late second trimester (after 20 weeks' gestation) of pregnancy.

## References


1. CDC. Preventing tetanus, diphtheria, and pertussis among adults: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP) and recommendation of ACIP, supported by the Healthcare Infection Control Practices Advisory Committee (HICPAC), for use of Tdap among health-care personnel. MMWR 2006;55(No. RR-17).
2. Healy CM, Rench MA, Castagnini LA, Baker CJ. Pertussis immunization in a high-risk postpartum population. Vaccine 2009;27:5599--602.
3. Healy CM, Rench MA, Baker CJ. Implementation of cocooning against pertussis in a high-risk population. Clin Infect Dis 2011;52:157--62.
4. CDC. Preventing tetanus, diphtheria, and pertussis among adolescents: use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccines. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2006;55(No. RR-3).
5. CDC. Updated recommendations for use of tetanus toxoid, reduced diphtheria toxoid and acellular pertussis (Tdap) vaccine from the Advisory Committee on Immunization Practices, 2010. MMWR 2011;60;13--5.
6. CDC. FDA approval of expanded age indication for a tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine. MMWR 2011;60;1279--80.
7. Gall SA, Myers J, Pichichero M. Maternal immunization with tetanus-diphtheria-pertussis vaccine: effect on maternal and neonatal serum antibody levels. Am J Obstet Gynecol 2011;204:334.e1--5.
8. Talbot EA, Brown KH, Kirkland, KB, Baughman AL, Halperin SA, Broder KP. The safety of immunizing with tetanus-diphtheria-acellular pertussis vaccine (Tdap) less than 2 years following previous tetanus vaccination: experience during a mass vaccination campaign of healthcare personnel during a respiratory illness outbreak. Vaccine 2010;28:8001--7.
9. Czeizel AE, Rockenbauer M. Tetanus toxoid and congenital abnormalities. Int J Gynecol Obstet 1999;64:253--8.
10. Silveria CM, Caceres VM, Dutra MG, Lopes-Camelo J, Castilla EE. Safety of tetanus toxoid in pregnant women: a hospital-based case-control study of congenital anomalies. Bull World Health Organ 1995;73:605--8.
11. Leuridan E, Hens N, Peeters N, de Witte L, Van der Meeren O, Van Damme P. Effect of a prepregnancy pertussis booster dose on maternal antibody titers in young infants. Pediatr Infect Dis J 2011;30:608--10.
12. Van Savage J, Decker MD, Edwards KM, Sell SH, Karzon DT. Natural history of pertussis antibody in the infant and effect on vaccine response. J Infect Dis 1990;161:487--92.

13. Ward JI, Cherry JD, Chang SJ, et al. *Bordetella pertussis* infections in vaccinated and unvaccinated adolescents and adults, as assessed in a national prospective randomized Acellular Pertussis Vaccine Trial (APERT). Clin Infect Dis 2006;43:151--7.
14. Van Rie A, Wendelboe AM, Englund JA. Role of maternal pertussis antibodies in infants. Pediatr Infect Dis J 2005;24(5 Suppl):S62--5.
15. Le T, Cherry JD, Chang SJ, et al. Immune responses and antibody decay after immunization of adolescents and adults with an acellular pertussis vaccine: the APERT study. J Infect Dis 2004;190:535--44.
16. Kirkland KB, Talbot EA, Decker MD, Edwards KM. Kinetics of pertussis immune responses to tetanus-diphtheria-acellular pertussis vaccine in health care personnel: implications for outbreak control. Clin Infect Dis 2009;49:584--7.
17. Englund JA, Anderson EL, Reed GF, et al. The effect of maternal antibody on the serologic response and the incidence of adverse reactions after primary immunization with acellular and whole-cell pertussis vaccines combined with diphtheria and tetanus toxoids. Pediatrics 1995;96(3 Pt 2):580--4.
18. Hardy-Fairbanks AJ, Pan SJ, Johnson DR, Bernstein HH. Immune responses in infants following receipt of pertussis immunization by their mothers during pregnancy. Presented at the 48th Infectious Diseases Society of America Annual Meeting, Vancouver, Canada; October 21--24, 2010.
19. Dalhousie University. Pertussis maternal immunization study. Identifier: NCT00553228. Available at http://clinicaltrials.gov/show/nct00553228 . Accessed October 13, 2011.
20. National Institute of Allergy and Infectious Diseases. Pertussis vaccine in healthy pregnant women. Identifier: NCT00707148. Available at http://clinicaltrials.gov/show/nct00707148 . Accessed October 13, 2011.
21. Halperin BA, Morris A, Mackinnon-Cameron D, et al. Kinetics of the antibody response to tetanus-diphtheria-acellular pertussis vaccine in women of childbearing age and postpartum women. Clin Infect Dis 2011;53:885--92.
22. Terranella A, Asay G, Messonnier M, Clark T, Liang J. Preventing infant pertussis: a decision analysis comparing prenatal vaccination to cocooning. Presented at the 49th Infectious Diseases Society of America Annual Meeting, Boston, MA; October 20--23, 2011.



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